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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/859,722	05/17/2001	William Stuart Somers	16163-004001 / AM100225	2770

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EXAMINER	
NOAKES, SUZANNE MARIE	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 03/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/859,722	SOMERS ET AL.	
	Examiner	Art Unit	
	Suzanne M. Noakes, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2001*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-35* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1 and 2, drawn to a crystallized P-selectin LE, classified in class 530, subclass 350.

II. Claims 3 and 4, drawn to a crystallized complex of P-selectin LE and SLe^x, classified in class 530, subclass 350.

III. Claims 5, 6 and 35, drawn to a crystallized complex of E-selectin LE and SLe^x and a method for obtaining a crystallized complex of an E-selectin type molecule and a compound that coordinates calcium by soaking a crystal of E-selectin in a PEG solution containing calcium, classified in class 530, subclass 350.

IV. Claims 7 and 8, drawn to a crystallized complex of P-selectin LE and PSGL-1, classified in class 530, subclass 350.

V. Claims 9 and 10, drawn to an active site of an SLe^x binding protein with calcium bound according to Fig. 3, classified in class 703, subclass 2.

VI. Claims 11 and 12, drawn to an active site of an SLe^x binding protein with calcium bound according to Fig. 4, classified in class 703, subclass 2.

VII. Claims 13 and 14, drawn to an active site of a PSGL-1 binding protein with strontium bound according to Fig. 5, classified in class 703, subclass 2.

VIII. Claim 15, drawn to an *in silico* methods of identifying agents that interact with P-selectin, classified in class 703, subclass 2.

IX. Claim 16, drawn to an *in vitro* methods of testing agents interact with P-selectin LE, classified in class 435, subclass 7.1.

X. Claim 17-19 and 26, drawn to an *in silico* methods of identifying agents that interact with a SLe^x binding site, classified in class 703, subclass 2.

XI. Claims 20, 21 and 27, drawn to an *in vitro* methods of testing agents interact with an SLe^x, classified in class 435, subclass 7.1.

XII. Claims 22-23 and 28, drawn to an *in silico* methods of identifying agents that interact with PSGL-1, classified in class 703, subclass 2.

XIII. Claims 24, 25 and 29, drawn to an *in vitro* methods of testing agents interact with an PSGL-1, classified in class 435, subclass 7.1.

XIV. Claim 30, drawn to an agent that interacts with P-selectin, classified in class 530, subclass 350.

XV. Claims 31 and 33, drawn to an inhibitor or activator of SLe^x, classified in class 530, subclass 350.

XVI. Claims 32 and 34, drawn to an inhibitor or activator of PSGL-1, classified in class 530, subclass 350.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I-IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are each drawn to a different crystal or crystal complex. Each different crystal requires its own different crystallization conditions, has its own unique

unit cell parameters which is determined by its space group and will have its own maximum resolution for diffraction. Thus each crystal is patentably distinct and a search for one crystal is by no mean coextensive with a search for another one in the protein crystallography electronic data bases (e.g. RSCB PDB) or for instance in the non-patent literature (e.g. Acta Cryst. D) which would place an undue search burden upon the examiner. For these reasons each group is separately and distinctly patentable.

3. Inventions V-VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are not disclosed as being capable of use together because each different active site is derived from a completely different crystal structure. Even though some amino acids of the active sites might be shared in common, each cartesian coordinate that defines the active site is not only derived differently, but each amino acid of the active sites will have different contacts. For example, the active site described in Figure 3 (Group V) will be completely different to that of Figure 4 (Group 4) because the former is ligand free whereas the later is bound to a calcium molecule. Furthermore, each different active site will change according the complex formed between the Sle^x protein and the protein that forms its complex, e.g. P-selectin in Group V, E-selectin in Group VI, PSGL-1 in Group VII. Thus, a search for one Group is not coextensive with any other Group and for this reason is proper so as not to place an undue search burden upon the examiner.

4. Inventions VIII, X and XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are drawn to *in silico* methods of identifying agents which bind to P-selectin (Group VIII), Sle^x binding proteins (Group X) or PSGL-1 (Group XII). Thus the methods are each separately drawn to completely different proteins which would require separate searches in the non-patent literature databases as well as the patent literature databases because each Group is derived from different proteins with their own unique active sites and overall structural coordinates. Thus, an under search burden would be expected of the examiner in order to search each Group. For these reasons, restriction is deemed as proper.

5. Inventions IX, XI and XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are each drawn to different *in vitro* assays which test whether or not potential agents are capable of modulating different proteins, e.g. P-selectin (Group IX), Sle^x binding proteins (Group XI) or PSGL-1 (Group XIII). Thus, each assay will use different components of the assay system, which would require separate and different searches in the non-patent and patent literature. Furthermore, each assay has completely different end points, for example, agents that modulate P-selectin likely will not have anything to do with agents that will modulate PSGL-1.

Therefore each different Group has its own respective distinct and separate patentable subject matter.

6. Inventions XIV-XVI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are drawn to agents, inhibitors or activators of P-selectin (Group XIV), Sle^x binding proteins (Group XV) or PSGL-1 (Group XVI). The Groups are deemed separately patentable because an activator or inhibitor or PSGL-1 will not have the same effects on Sle^x because each different protein has its own unique activation or binding site which will be structurally unique for only those molecules which can fit into its binding site. One that works for one Group will likely not work for another. Furthermore, each agent, activator or inhibitor will have its own unique structure and function, distinct and separate from those of the other Groups. Thus a search for one Group is not co-extensive for a search for any other Group and for these reasons restriction is deemed proper.

7. Inventions (I-IV) and (V-VII) are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the active sites Groups V-VII does not directly use the products (e.g. the crystals of P-selectin, P-selectin:Sle^x, E-selectin:Sle^x and P-selectin LE:PSGL-1) of groups I-IV. Instead Groups V-VII are merely the atomic coordinates of the active sites of P-selectin:Sle^x, E-

selectin:Sle^x and P-selectin LE:PSGL-1 and is only related to the crystal product of P-selectin, P-selectin:Sle^x, E-selectin:Sle^x and P-selectin LE:PSGL-1 by being a tangible and artificial representation of the physical atomic level structure. Thus the crystal Groups and active site Groups are not directly utilizable together, nor are they disclosed as being capable as such.

8. Inventions (I-IV) and (VIII, X, XII) are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the *in silico* method of identifying agents of Groups VIII, X, XII does not directly use the products (e.g. the crystals of P-selectin, P-selectin:Sle^x, E-selectin:Sle^x and P-selectin LE:PSGL-1) of groups I-IV. Instead Groups VIII, X, XII utilizes the atomic coordinates of P-selectin, P-selectin:Sle^x, E-selectin:Sle^x and P-selectin LE:PSGL-1 in the design process and is only related to the crystal product of P-selectin, P-selectin:Sle^x, E-selectin:Sle^x and P-selectin LE:PSGL-1 by being a tangible and artificial representation of the physical atomic level structure. Thus the crystal Groups and *in silico* Groups are not directly utilizable together, nor are they disclosed as being capable as such.

9. Inventions (I-IV) and (IX, XI, XIII) are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the Groups of the *in vitro* methods of identifying agents, activators or inhibitors of P-selectin, Sle^x

and PSGL-1 use a completely different physical form (and patentably distinct form) of these proteins. The crystalline forms of are not capable of being used in an *in vitro* assay because if one did so it would result in the destruction of the crystal structure all together.

10. Inventions (I-IV) and (XIV-XVI) are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions the crystals of Groups (I-IV) the agents, activators or inhibitors of Groups XIV-XVI have completely different structure, function and form. The proteins found within the crystals bear no structural or functional similarities with the activators or inhibitors which may or may not interact upon the proteins found in each crystal. Furthermore, the crystal Groups and the agents Groups are not disclosed as being capable of being used together.

11. Inventions (V-VII) and (VII, X, XII) are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct if they do not overlap in scope and are not obvious variants, and if it is shown that at least one subcombination is separately usable. In the instant case, subcombination of *in silico* methods of using the atomic coordinates defined by the active sites has separate utility such as specific drug design. Alternatively, the active sites atomic coordinates can be used to define a specific pharmacophore. See MPEP § 806.05(d).

12. Inventions (V-VII) and (IX, XI, XIII) are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have

different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are capable as being used together. The active site Groups are defined only by three-dimensional atomic coordinates. Thus it would be physically impossible to use the *in vitro* assay Groups because these Groups utilizes physical organic molecules, which would be impossible to combine with empirical data which defines the active sites of Groups V-VII.

13. Inventions (V-VII) and (XIV-XVI) are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are capable as being used together. The active site Groups are defined only by three-dimensional atomic coordinates. Thus it would be physically impossible to use a physical organic molecule such as those of the of the agents, activator and inhibitor Groups (XIV-XVI) with empirical data which defines the active sites of Groups V-VII.

14. Inventions (VIII, X, XII) and (IX, XI, XIII); (XIV-XVI) are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions the Groups of the *in silico* methods utilize only empirical data in its operation and method steps. However, the Groups of the *in vitro* methods use physically defined, real world organic material. Thus, there is no way to actually physically use the different Groups together. The same analogy can be applied to the agents, activators and modulators Groups (XIV-XVI); the *in silico*

methods Groups again utilize empirical data confined within a computer and can not be extended or combined with physical organic material.

15. Inventions (IX, XI, XIII) and (XIV-XVI) are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions the method steps utilized in the *in vitro* assay Groups (IX, XI, XIII) have different designs and method steps which may or may not utilize the agents, activators or inhibitors of Groups (XIV-XVI). Thus, a search for the *in vitro* assays and components defined within each will not necessarily be coextensive. Furthermore, the data bases searched will be completely separate in both the structural and non-patent literature databases. This would place an undue search burden upon the examiner.

Potential Right to Rejoinder

16. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

17. Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

18. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suzanne M. Noakes, Ph.D. whose telephone number is 571-272-2924. The examiner can normally be reached on Monday to Friday, 7.30am to 4.00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SMN
20 March 2006

KATHLEEN M. KERR, PH.D.
SUPERVISORY PATENT EXAMINER